REMARKS

Status of the Claims

Claims 1-24 and 27-43 are now pending in the present application, Claims 25 and 26 having been canceled herein, and new Claims 29-43 having been added. Claims 1-3, 8-10, 16-18, and 27 have been amended to more clearly define the subject matter being claimed.

Telephone Interview

In February 2010, Examiner Heidemann and applicants' attorney (Michael King, Registration No. 44,832) conducted a Telephone Interview to discuss the pending claims.

The discussion focused on how the claims distinguished over applicants' earlier filed applications, which have been employed as primary references in rejecting the claims (the Basiji and Ortyn references).

The Examiner suggest language directed to classification of cells might be helpful in distinguishing the subject matter being claimed.

No agreement as to the patentability of the claims was reached.

Applicants would like to thank the Examiner for his time and willingness to discuss the application in the above-mentioned Telephone Interview.

Rejection under 35 U.S.C. § 112

Claim 16 has been rejected 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

More specifically, the Examiner notes that there is a lack of antecedent basis for the nuclear marker image and the cell image.

Claim 16 has been amended to provide antecedent basis for the nuclear marker image element.

Claim 16 has also been amended to provide antecedent basis for the spatial frequency content element.

Applicants respectfully submit that there is no indefiniteness issue with respect to the cell image limitation, because the claim does recite using *a detector to obtain an image of the cell.* While the italicized recitation is not identical to the term *cell image*, applicants respectfully submit that the artisan of ordinary skill would readily understand that the term cell image clearly referred to the image obtained using the recited detector.

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MPEP 2173.05(e) clearly indicates that *the failure to provide explicit antecedent basis for terms does not always render a claim indefinite. If the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite*. While it is correct that there is no explicit antecedent basis for the term *cell image*, applicants respectfully submit that because the claim clearly recites using a detector to obtain an image of a cell, the artisan of ordinary skill would be able to readily ascertain the scope of the term cell image.

Claims Rejected under 35 U.S.C. § 102(b) over Basiji '955

Claims 1, 2, 3, 26/1, 26/2, and 26/3 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Basiji (U.S. Patent Number 6,211,955).

In the interest of reducing the complexity of the issues for the Examiner to consider in this response, the following discussion focuses on independent Claim 1. The patentability of each remaining dependent claim is not necessarily separately addressed in detail. However, applicants' decision not to discuss the differences between the cited art and each dependent claim should not be considered as an admission that applicants concur with the Examiner's conclusion that these dependent claims are not patentable over the disclosure in the cited references. Similarly, applicants' decision not to discuss differences between the prior art and every claim element, or every comment made by the Examiner, should not be considered as an admission that applicants concur with the Examiner's interpretation and assertions regarding those claims. Indeed, applicants believe that all of the dependent claims patentably distinguish over the references cited. In any event, a specific traverse of the rejection of each dependent claim is not required, since dependent claims are patentable for at least the same reasons as the independent claims from which the dependent claims ultimately depend.

Patentability of Independent Claim 1

Independent Claim 1 as amended recites:

A method for identifying a specific cell, to enable a determination to be made as to whether the specific cell corresponds to a known cell type, comprising the steps of:

providing spatial frequency content data from a side scatter image of the known cell type;

directing incident light at the specific cell, using a detector to obtain the side scatter image of the specific cell; and

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comparing the spatial frequency content of the side scatter image of the specific cell to the spatial frequency content data of the side scatter image of the known cell type to determine if the specific cell corresponds to the known cell type.

Applicants recognize that the Basiji reference does disclose an imaging system that can be used to acquire a side scatter image of a cell, and that the Basiji reference specifically discloses determining the spatial frequency content of a side scatter image. The Basiji reference also discloses that morphological, photometric, and spectral characteristics of cells can be measured using image data collected from the imaging system disclosed in that reference.

However, the Basiji reference ***does not*** teach or suggest that the spatial frequency content of the side scatter image can be used to specifically identify a particular cell. It is clear that the Basiji reference recognizes that the spatial frequency content of the side scatter image can be collected, along with various other metrics. But the Basiji reference simply does not teach that the spatial frequency content of a side scatter image of a cell can be used to uniquely identify a particular cell. In other words, the Basiji reference does not teach or suggest that different cell types can be distinguished from one another based on the spatial frequency content of the side scatter image from each cell.

The Basiji reference does disclose in detail a particular type of cellular analysis for which the disclosed imaging system can be used. That particular analysis is detecting the presence and composition of Fluorescence *In-Situ* Hybridization (FISH) probes within cells, which is discussed in detail in the Basiji reference in connection with the description of FIGURE 16. However, there simply is no mention in the Basiji reference that the spatial frequency content of a side scatter image of the cell can be used to differentiate one type of cell from another. ***That concept goes well beyond the scope of the disclosure in the Basiji reference.***

Essentially, the Basiji reference teaches a unique imaging system that can be used to collect images of objects such as cells, and those images can be analyzed to determine many different metrics. The spatial frequency content metric is specifically identified. Significantly, the Basiji reference specifically discloses that many different metrics can be collected, including nuclear area, perimeter, texture or spatial frequency content, centroid position, shape, volume, and ratios of such parameters. However, the Basiji reference does not teach or suggest that any of those metrics individually can be used to specifically identify one cell type from another cell type; much less teaching that the spatial

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frequency content of a side scatter image alone can be used to identify a first cell type from a second cell type.

Because dependent claims inherently include each element recited in the independent claim upon which they ultimately depend, each claim depending upon independent Claim 1 is patentable for at least the same reasons as those discussed above. Accordingly, the rejection of dependent Claims 2 and 3 under 35 U.S.C. § 102(b) as being anticipated by Basiji should also be withdrawn. Claim 26 has been canceled.

Claims Rejected under 35 U.S.C. § 102(b) over Ortyn

Claims 8, 9, 10, 15, 26/8, 26/10, and 26/15 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Ortyn (U.S. Patent Publication Number 2002/0071121).

In the interest of reducing the complexity of the issues for the Examiner to consider in this response, the following discussion focuses on independent Claim 8. The patentability of each remaining dependent claim is not necessarily separately addressed in detail. However, applicants' decision not to discuss the differences between the cited art and each dependent claim should not be considered as an admission that applicants concur with the Examiner's conclusion that these dependent claims are not patentable over the disclosure in the cited references. Similarly, applicants' decision not to discuss differences between the prior art and every claim element, or every comment made by the Examiner, should not be considered as an admission that applicants concur with the Examiner's interpretation and assertions regarding those claims. Indeed, applicants believe that all of the dependent claims patentably distinguish over the references cited. In any event, a specific traverse of the rejection of each dependent claim is not required, since dependent claims are patentable for at least the same reasons as the independent claims from which the dependent claims ultimately depend.

Patentability of Independent Claim 8

Independent Claim 8 as amended recites:

A method for identifying a specific cell, to enable a determination to be made as to whether the specific cell corresponds to a known cell type comprising the steps of:

providing spatial frequency content data from a brightfield image of the known cell type;

directing incident light at the specific cell, using a detector to obtain the brightfield image of the specific cell; and

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comparing the spatial frequency content of the brightfield image of the specific cell to the spatial frequency content data of the brightfield image of the known cell type to determine if the specific cell corresponds to the known cell type.

Applicants recognize that the Ortyn reference does disclose an imaging system that can be used to acquire a brightfield image of a cell, and that the Ortyn reference specifically discloses determining the spatial frequency content of a brightfield image. The Ortyn reference also discloses that morphological, photometric, and spectral characteristics of cells can be measured using image data collected from the imaging system disclosed in that reference.

However, the Ortyn reference does not teach or suggest that the spatial frequency content of the brightfield image can be used to specifically identify a particular cell. It is clear that the Ortyn reference recognizes that the spatial frequency content of the brightfield image can be collected, along with various other metrics. But the Ortyn reference simply does not teach that the spatial frequency content of a brightfield image of a cell can be used to uniquely identify a particular cell. In other words, the Ortyn reference does not teach or suggest that different cell types can be distinguished from one another based on the spatial frequency content of the brightfield image from each cell.

The Ortyn reference does disclose in detail a particular type of cellular analysis for which the disclosed imaging system can be used. That particular analysis is detecting the presence and composition of Fluorescence *In-Situ* Hybridization (FISH) probes within cells, which is discussed in detail in the Ortyn reference in connection with the description of FIGURE 16. However, there simply is no mention in the Ortyn reference that the spatial frequency content of a brightfield image of the cell can be used to differentiate one type of cell from another. That concept goes well beyond the scope of the disclosure in the Ortyn reference.

Another way of looking at this issue is that applicants' earlier applications (the Basiji and Ortyn references) disclosed the development of a novel imaging system that could be used to collect many different metrics about objects such as cells. Those metrics could be used for analysis of cells, and one specifically disclosed analysis is the FISH analysis noted above. However, there simply is no recognition in the Basiji or Ortyn references as to what particular metrics that could be collected by the novel imaging system would be useful in specifically identifying one type of cell from another. To determine that different cellular types could be distinguished from one another, applicants had to use the novel imaging system to collect data from different types of cells, and then compare the various

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metrics for each type of cell to determine which of the plurality of different metrics individually or in combination with other metrics could be used to differentiate the cell types. Until that analysis was performed, it was not known, and was not obvious, what metrics would enable such differentiation to be performed. Simply knowing that a pool of metrics are to be collected does not indicate which of the metrics can be employed for a specific purpose (such as uniquely identifying cell type).

Because dependent claims inherently include each element recited in the independent claim upon which they ultimately depend, each claim depending upon independent Claim 8 is patentable for at least the same reasons as those discussed above. Accordingly, the rejection of dependent Claims 9, 10, and 15 under 35 U.S.C. § 102(b) as being anticipated by Ortyn should also be withdrawn. Claim 26 has been canceled.

Claims Rejected under 35 U.S.C. § 102(b) over Rosania

Claims 16, 17, 18, 23, 25/16, 25/17, and 25/23 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Rosania (U.S. Patent Publication Number 2003/0059093).

In the interest of reducing the complexity of the issues for the Examiner to consider in this response, the following discussion focuses on independent Claim 16. The patentability of each remaining dependent claim is not necessarily separately addressed in detail. However, applicants' decision not to discuss the differences between the cited art and each dependent claim should not be considered as an admission that applicants concur with the Examiner's conclusion that these dependent claims are not patentable over the disclosure in the cited references. Similarly, applicants' decision not to discuss differences between the prior art and every claim element, or every comment made by the Examiner, should not be considered as an admission that applicants concur with the Examiner's interpretation and assertions regarding those claims. Indeed, applicants believe that all of the dependent claims patentably distinguish over the references cited. In any event, a specific traverse of the rejection of each dependent claim is not required, since dependent claims are patentable for at least the same reasons as the independent claims from which the dependent claims ultimately depend.

Patentability of Independent Claim 16

Independent Claim 16 as amended recites:

A method for identifying a specific cell, to enable a determination to be made as to whether the specific cell corresponds to a known cell type comprising the steps of:

providing an image of the known cell type that has been marked with a nuclear marker;

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providing spatial frequency content data from the image of the known cell type that has been marked with the nuclear marker;

contacting the specific cell with the nuclear marker;

directing incident light at the marked specific cell;

using a detector to obtain an image of the marked specific cell; and

comparing the image of the marked specific cell and a spatial frequency content of the image of the marked specific cell to the marked image of the known cell and the spatial frequency content of the marked image of the known cell type to determine if the specific cell corresponds to the known cell type.

Applicants recognize that the Rosania reference does disclose using a nuclear marker and collecting images of cells, and analyzing those images to differentiate cells. In particular, Rosania discloses that the microtubule levels in a nucleus can be measured, and that different microtubule levels could be used to identify specific cell types. In paragraph [0080], Rosania discloses three cell types; control cells (microtubule levels unchanged), cells treated with nocodazole (microtubule levels decreased), and cells treated with paclitaxel (which appears to increase microtubule levels). In paragraph [0078] Rosania teaches that the microtubules are stained with a marker, and in paragraph [0079] images are acquired. Significantly, in paragraph [0080] Rosania discloses the image analysis involves generating a binary nuclear mask by thresholding a Hoechst image, and dilating the nuclear image to produce a perinuclear ring mask. The *intensity* of the stained microtubules could then be measured from the perinumclear ring mask. The differentiation is based on separating the cells into three groups; cells with relatively low amounts of microtubules (which correspond to cells treated with a first reagent known to decrease microtubule content), cells with relatively high amounts of microtubules (which correspond to cells treated with a second reagent known to increase microtubule content), and cells with levels of microtubules in between the relatively lower microtubule content group and the relatively higher microtubule content group (which correspond to control or untreated cells).

Significantly, Rosania does not *provide an image of the known cell type that has been marked with a nuclear marker* and *provide spatial frequency content data from the image of the known cell type that has been marked with the nuclear marker*, nor does Rosania compare those provided data points with the empirically collected data to separate or classify the cells into different groups. The techniques are somewhat related, but differ in their implementation, and this is not equivalent. Nor does there

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appear to be any reason for the artisan of ordinary skill to modify Rosania's technique to achieve an equivalent.

Because dependent claims inherently include each element recited in the independent claim upon which they ultimately depend, each claim depending upon independent Claim 16 is patentable for at least the same reasons as those discussed above. Accordingly, the rejection of dependent Claims 17, 18, and 23 under 35 U.S.C. § 102(b) as being anticipated by Rosania (U.S. Patent Publication Number 2003/0059093) should also be withdrawn. Claim 25 has been canceled.

Claims Rejected under 35 U.S.C. § 102(b) over Ortyn

Claim 27 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Yarosalvsky (U.S. Patent Publication Number 2005/0094147).

Independent Claim 27 as amended recites:

A kit for use in a multispectral imaging system to identify a specific cell, comprising a single nuclear marker, wherein a cell is contacted with the single nuclear marker for a time sufficient to allow identification of an apoptotic cell or a necrotic cell with the multispectral imaging system using only a single nuclear marker.

With respect to Yarosalvsky, applicants respectfully submit that the reference does not appear to disclose a nuclear marker. The artisan of ordinary skill in the art will readily recognize that the term nuclear marker refers to a fluorescent agent that will bind to a component in the nucleus of a cell. Yarosalvsky clearly discloses fluorescent markers, however, Yarosalvsky's fluorescent markers can be characterized by their preferential absorption by cancer tissue as opposed to healthy tissue (see paragraph [0096]). There is simply no basis to conclude that Yarosalvsky's fluorescent markers preferentially bind to cellular material found in the nucleus.

Furthermore, it must be understood that applicants' nuclear marker will attach itself to nuclear material only if the nuclear membrane is compromised, or some of the nuclear material itself undergoes translocation. For example, annexin V is a nuclear marker that preferentially binds to phosphatidylserine (PPS), found in the nucleus of healthy cells, but translocating out of the nucleus during apoptosis. 7-aminoactinomycin D is a nuclear marker that attaches itself to the nuclear material of necrotic and apoptotic cells after the nuclear membrane loses its integrity. Yarosalvsky's fluorescent markers are NOT only marking apoptotic or necrotic cells, they are also marking viable cancer cells as well.

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When annexin V and 7-aminoactinomycin D are used together, viable cells, cells undergoing early stage apoptosis, and cells undergoing late stage apoptosis can be differentiated. Viable cells will have no marking, because the nuclear membrane is intact (the markers cannot enter the nucleus) and no translocation of PPS will have occurred. Cells undergoing early stage apoptosis will only be marked with annexin V, because the nuclear membrane is intact (the markers cannot enter the nucleus), but translocation of PPS will have occurred. Cells undergoing late stage apoptosis will be marked with both markers, because the nuclear membrane is no longer intact (the markers can enter the nucleus). Significantly, cells undergoing late stage apoptosis cannot be differentiated from necrotic cells using these two markers, as both markers will be present in late stage apoptotic cells and necrotic cells because the nuclear membrane is no longer intact.

Claim 27 is novel because only one nuclear marker is used to differentiate between apoptotic cells and necrotic cells, which is not possible using prior art techniques. A kit with a plurality of markers would be known, but not with only a single marker capable of differentiating apoptotic cells and necrotic cells. Applicants' technique involves using fluorescent data combined with brightfield image data and darkfield image data, to enable viable, necrotic, and apoptotic cells to be distinguished while using only a single nuclear marker.

Claims Rejected under 35 U.S.C. § 103(b)

Claims 4, 7, 26/4, and 27/4 have been rejected as being obvious over Basiji in view of Kim (U.S. Patent Publication Number 2003/0040031).

Claim 26 has been canceled.

Claims 4 and 7 depend on Claim 1, which has been significantly amended. In its amended form, Claim 1 distinguishes over Basiji, as discussed in detail above. Kim provides no teaching that would cure the deficiency of Basiji with respect to Claim 1 in its amended form, thus Claim 1 distinguishes over such a combination, and all claims depending upon Claim 1 are patentable for at least the same reasons.

Claims 11, 14, 19, 22, 26/11, and 26/14 have been rejected as being obvious over Ortyn in view of Kim (U.S. Patent Publication Number 2003/0040031).

Claim 26 has been canceled.

Claims 11 and 14 depend on Claim 8, which has been significantly amended. In its amended form, Claim 8 distinguishes over Ortyn, as discussed in detail above. Kim provides no teaching that

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would cure the deficiency of Ortyn with respect to Claim 8 in its amended form, thus Claim 8 distinguishes over such a combination, and all claims depending upon Claim 8 are patentable for at least the same reasons.

Claims 19 and 22 depend on Claim 16, which has been significantly amended. In its amended form, Claim 16 distinguishes over Ortyn, as discussed in detail above. Kim provides no teaching that would cure the deficiency of Ortyn with respect to Claim 16 in its amended form, thus Claim 16 distinguishes over such a combination, and all claims depending upon Claim 16 are patentable for at least the same reasons.

Claims 4, 5, 6, 7, 26/4, 26/5, 26/6, and 26/7 have been rejected as being obvious over Basiji in view of Rich (U.S. Patent Publication Number 2001/0012620).

Claim 26 has been canceled.

Claims 4, 5, 6, and 7 depend on Claim 1, which has been significantly amended. In its amended form, Claim 1 distinguishes over Basiji, as discussed in detail above. Rich provides no teaching that would cure the deficiency of Basiji with respect to Claim 1 in its amended form, thus Claim 1 distinguishes over such a combination, and all claims depending upon Claim 1 are patentable for at least the same reasons.

Furthermore, applicants respectfully point out that Rich employs a fundamentally different analysis than recited in Claim 1, which requires the analysis be based on *spatial frequency content data* acquired from an image. Rich employs two different techniques (flow cytometry [0112] and fluorescence microscopy [0113] to measure the pH of cells, and using the different pH values to differentiate cells (see [0109]-[0111]). The pH analysis appears to be based on using a fluorescence ratio. It is not apparent that Rich even measures a *spatial frequency content* of a side scatter image of a cell. Accordingly, even if Basiji were modified in view of Rich, the analysis of apoptotic cells would be based on using fluorescence to measure pH, not on the *spatial frequency content* parameter.

Claims 11, 12, 13, 14, 26/11, 26/12, 26/13, and 26/14 have been rejected as being obvious over Ortyn in view of Rich (U.S. Patent Publication Number 2001/0012620).

Claim 26 has been canceled.

Claims 11, 12, 13, and 14 depend on Claim 1, which has been significantly amended. In its amended form, Claim 1 distinguishes over Ortyn, as discussed in detail above. Rich provides no teaching that would cure the deficiency of Ortyn with respect to Claim 1 in its amended form, thus

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Claim 1 distinguishes over such a combination, and all claims depending upon Claim 1 are patentable for at least the same reasons.

Furthermore, applicants respectfully point out that Rich employs a fundamentally different analysis than recited in Claim 1, which requires the analysis be based on *spatial frequency content data* acquired from an image. Rich employs two different techniques (flow cytometry [0112] and fluorescence microscopy [0113] to measure the pH of cells, and using the different pH values to differentiate cells (see [0109]-[0111]). The pH analysis appears to be based on using a fluorescence ratio. It is not apparent that Rich even measures a *spatial frequency content* of a side scatter image of a cell. Accordingly, even if Ortyn were modified in view of Rich, the analysis of apoptotic cells would be based on using fluorescence to measure pH, not on the *spatial frequency content* parameter.

Claims 19, 20, 21, 22, 25/19, 25/21, and 25/22 have been rejected as being obvious over Rosania in view of Rich (U.S. Patent Publication Number 2001/0012620).

Claim 25 has been canceled.

Claims 19, 20, 21, and 22 depend on Claim 16, which has been significantly amended. In its amended form, Claim 16 distinguishes over Rosania, as discussed in detail above. Rich provides no teaching that would cure the deficiency of Rosania with respect to Claim 16 in its amended form, thus Claim 16 distinguishes over such a combination, and all claims depending upon Claim 16 are patentable for at least the same reasons.

Claims 24 and 25/24 have been rejected as being obvious over Rosania in view of Fraatz (U.S. Patent No. 5,372,936).

Claim 25 has been canceled.

Claim 24 depends on Claim 16, which has been significantly amended. In its amended form, Claim 16 distinguishes over Rosania, as discussed in detail above. Fraatz provides no teaching that would cure the deficiency of Rosania with respect to Claim 16 in its amended form, thus Claim 16 distinguishes over such a combination, and all claims depending upon Claim 16 are patentable for at least the same reasons.

Claims 26/16, 26/17, 26/18, and 26/23 have been rejected as being obvious over Rosania in view of Basiji.

Claim 26 has been canceled.

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Claims 26/19, 26/20, 26/21, and 26/22 have been rejected as being obvious over Rosania in view of Rich and Basiji.

Claim 26 has been canceled.

Claims 26/24 has been rejected as being obvious over Rosania in view of Fraatz and Basiji.

Claim 26 has been canceled.

Claim 28 has been rejected as being obvious over Yarosalvsky in view of Fraatz and Basiji.

Claim 28 depends on Claim 27, which has been amended. In its amended form, Claim 27 distinguishes over the cited art.

Patentability of Newly Added Claims

Claims 29-43 have been added to further define the subject matter being claimed. The originally presented claims are clearly directed to identifying apoptotic cells and necrotic cells from images of cells, and the new claims presented herein define the technique with more specificity. The elements of the newly added claims relate to the subject matter disclosed in paragraphs [0044]-[0048].

Prior art techniques for identifying apoptotic cells and necrotic cells are provided by Rich at paragraphs [0132] and [0133]. Significantly, these prior art techniques are based on collecting fluorescent data from cells exposed to various combinations of fluorescent markers. Claims 29-43 use other cell parameters (i.e., parameters in addition to fluorescence) to classify cells according to the viability of the cell. The cited art does not appear to teach combining such other parameters with fluorescence. Significantly, applicants' technique enables the classification to be achieved using only a single nuclear marker.

Claim 29 distinguishes over the cited art because the cited art uses fluorescence alone to identify necrotic or apoptotic cells. Claim 29 employs data from a fluorescent image combined with data from at least one of a brightfield image and a darkfield image to determine the viability status of the specific cell, wherein the viability status corresponds to a first status indicating that the specific cell is a viable cell, a second status indicating that the specific cell is in a relatively early stage of apoptosis, a third status indicating that the specific cell is in relatively late stage of apoptosis, and a fourth status indicating that the specific cell is a necrotic cell.

Claim 30 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as a viable cell if the cell exhibits a relatively larger cellular area as determined from

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the brightfield image and no nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 31 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as a viable cell if the cell exhibits a relatively lower scatter peak intensity as determined from the darkfield image and no nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 32 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as a viable cell if the cell exhibits a relatively larger cellular area as determined from the brightfield image, a relatively lower scatter peak intensity as determined from the darkfield image, and no nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 33 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as being in an early stage of apoptosis if the cell exhibits a relatively smaller cellular area as determined from the brightfield image and no nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 34 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as being in an early stage of apoptosis if the cell exhibits a relatively higher scatter peak intensity as determined from the darkfield image and no nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 35 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as being in an early stage of apoptosis if the cell exhibits a relatively smaller cellular area as determined from the brightfield image, a relatively higher scatter peak intensity as determined from the darkfield image, and no nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 36 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as being in a late stage of apoptosis if the cell exhibits a relatively smaller cellular area as determined from the brightfield image and the nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 37 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as being in a late stage of apoptosis if the cell exhibits a relatively higher scatter peak

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intensity as determined from the darkfield image and the nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 38 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as being in a late stage of apoptosis if the cell exhibits a relatively smaller cellular area as determined from the brightfield image, a relatively higher scatter peak intensity as determined from the darkfield image, and the nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 39 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as being necrotic if the cell exhibits a relatively larger cellular area as determined from the brightfield image and the nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 40 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as being necrotic if the cell exhibits a relatively lower scatter peak intensity as determined from the darkfield image and the nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 41 distinguishes over the cited art because the cited art does not teach or suggest identifying a cell as being necrotic if the cell exhibits a relatively larger cellular area as determined from the brightfield image, a relatively lower scatter peak intensity as determined from the darkfield image, and the nuclear marker is present in the cell nucleus as determined by the fluorescent image.

Claim 42 distinguishes over the cited art because the cited art does not teach or suggest analyzing an image a cell to look for blebbing in combination with looking for nuclear markers in a fluorescent image to determine a viability of the cell.

Claim 43 distinguishes over the cited art because the cited art does not teach or suggest analyzing an image of a cell to look for blebbing in combination with looking for nuclear markers in a fluorescent image to determine a viability of the cell, such that:

when no blebbing is determined to be present by analyzing the brightfield image, and no nuclear marker is determined to be present in the cellular nucleus by analyzing the fluorescent image, it can be concluded that the viability status of the cell corresponds to the first status indicating that the specific cell is viable;

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when blebbing is determined to be present by analyzing the brightfield image, and no nuclear marker is determined to be present in the cellular nucleus by analyzing the fluorescent image, it can be concluded that the viability status of the cell corresponds to the second status indicating that the specific cell is in a relatively early stage of apoptosis;

when blebbing is determined to be present by analyzing the brightfield image, and the nuclear marker is determined to be present in the cellular nucleus by analyzing the fluorescent image, it can be concluded that the viability status of the cell corresponds to the third status indicating that the specific cell is in a relatively late stage of apoptosis; and

when no blebbing is determined to be present by analyzing the brightfield image, and nuclear marker is determined to be present in the cellular nucleus by analyzing the fluorescent image, it can be concluded that the viability status of the cell corresponds to the fourth status indicating that the specific cell is necrotic.

Conclusion

In consideration of the amendment to the claims and the Remarks set forth above, it is applicants' position that all claims in the current application are patentable over the art of record. The Examiner is thus requested to pass this case to issue without further delay. In the event that any other issues remain, the Examiner is invited to telephone applicants' attorney at the number listed below.

Respectfully submitted,

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